

ABSTRACTS

This section of the JOURNAL is published in collaboration with the two abstracting Journals, ABSTRACTS OF WORLD MEDICINE and OPHTHALMIC LITERATURE, published by the British Medical Association. The abstracts are divided into the following sections: Syphilis, (Clinical, Therapy, Serology, Pathology, Experimental), Gonorrhoea, Non-gonococcal Urethritis and Allied Conditions, Chemotherapy, Public Health and Social Aspects, Miscellaneous. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.

SYPHILIS (Clinical)

Fijian Syphilis. MANSON-BAHR, P. E. C. (1954). *Trans. roy. Soc. trop. Med. Hyg.*, **48**, 242. 26 refs.

(1) Three cases of congenital, two of primary, and one of meningovascular syphilis are described in Fijians and a Fijian-Tongan.

(2) Experimental and clinical evidence is brought forward to show that the previous absence of recorded syphilis in Fijians favours the existence among communities in whom yaws is prevalent, of a relative immunity to naturally acquired syphilis.

(3) This relative immunity is breaking down in Fiji as the result of successful yaws treatment in the past.

[Author's summary]

Pupillary Disturbances encountered in Medical Affections Statistics of 2,121 Cases. OKINAKA, S., TOYOKURA, Y., TSUBAKI, T., KUROIWA, Y., HIKOSAKA, R., MOZAI, B., and NAKAMURA, H. (1953). *Folia psychiat. neurol. jap.*, **7**, 161. 13 tables, 5 refs.

Pupillary disturbances were found in 347 cases (16.4 per cent.), made up as follows: reflex disturbance in 11.3 per cent., anisocoria in 9.3 per cent., irregularity of shape in 4.3 per cent., and disturbance in accommodation in 1.2 per cent.

Syphilitic, particularly neurosyphilitic, diseases caused most pupillary disturbances, then cases with a syphilitic history, and then non-syphilitic diseases, the ratio being approximately 6:3:1.

Absolute loss of pupillary reflex was found in ten cases, seven of which were neurological diseases, and three of diabetes mellitus.

A true Argyll Robertson pupil was observed in eighteen cases, twelve of which were syphilitic.

The pupillary disturbances found in non-syphilitic diseases were chiefly observed in neurological cases, but fairly often in tumours of the liver, oesophageal tumour, cholecystopathies, cancer of the stomach, pleurisy, typhoid fever, and pulmonary tuberculosis. H. Hagiwara

Ocular Examination in Diagnosis of Congenital Syphilis.

GROSS, B. A., and MEYER, G. P. (1954). *Amer. J. Syph.*, **38**, 30. 12 figs.

The ocular signs are interstitial keratitis, iris atrophy, chorio-retinitis, perivasculitis, and optic atrophy. The authors describe these signs in detail, distinguishing four types of chorio-retinitis. The value of slit-lamp examination and perimetry is discussed. M. H. T. Yuille

Investigation of Syphilis during Pregnancy. (Ergebnisse bei Schwangerenuntersuchungen auf Syphilis.) WOLFRAM, G. (1954). *Derm. Wschr.*, **129**, 623.

Pseudotumoral Syndrome. Syphiloma of the Pancreas—14-Year Control. CASTIGLIANO, S. G. (1954). *Amer. J. Roentgenol.*, **72**, 45. 3 figs, 39 refs.

Acute Meningovascular Syphilis during the Poliomyelitis Season. SASLAW, S., and SAKOL, M. (1954). *Ohio St. med. J.*, **50**, 665. 2 refs.

Special Problems in the Diagnosis and Management of Syphilis in Military Personnel. REIN, C. R., KOSTANT, G. H., and KIMMELMAN, J. A. (1954). *U.S. armed Forces med. J.*, **5**, 939. 19 refs.

SYPHILIS (Therapy)

Comparative Sensitivity of Treponemes of Syphilis, Yaws, and Bejel to Penicillin in vitro, with Observations on Factors affecting its Treponemicidal Action. NELL, E. E. (1954). *Amer. J. Syph.*, **38**, 92. 4 figs, 29 refs.

At the International Treponematoses Laboratory Center, Baltimore, seven strains of *Treponema pallidum*, two of *T. pertenue*, and three of bejel treponemata were exposed to varying concentrations of penicillin at 35° C. for 18 hours and the effect on motility observed as an indication of antitreponemal efficacy. No difference in susceptibility to penicillin was found between the strains tested. A five- to six-fold variation in the number of organisms in the inoculum did not influence

the results, but the activity of penicillin increased with rising temperature between 25 and 35° C. With a concentration of penicillin of 0.001 µg. per ml. or less no effect on the motility of the organisms was observed. Above this concentration the rate of immobilization of the treponemes increased directly with the penicillin concentration up to a maximum of 0.1 µg. per ml., beyond which little further increase occurred. The further study of many strains is desirable to determine whether penicillin resistance, natural or acquired, occurs in treponemes.

G. W. Csonka

Treatment of Early Infectious Syphilis with N:N'-Dibenzylethylenediamine Dipenicillin G. SMITH, C. A., O'BRIEN, J. F., SIMPSON, W. G., HARB, F. W., and SHAFER, J. K. (1954). *Amer. J. Syph.*, **38**, 136. 2 figs, 4 refs.

At three different venereal disease clinics in the U.S.A. 127 patients, twenty with sero-negative primary syphilis, 25 with sero-positive primary syphilis, and 82 with secondary syphilis, were treated with a single injection of 2.5 mega units of "Bicillin" (N:N'-dibenzylethylenediamine dipenicillin G). Of these, 86 have been observed for at least 6 months and fifty for more than one year.

All twenty of those originally sero-negative were still sero-negative at the last examination. At the end of 6 months 81 per cent. of those with sero-positive primary syphilis and 65 per cent. of the secondary cases were sero-negative, and at one year the sero-negativity curves were similar to those of other successfully treated series. The cumulative re-treatment rate at 12 to 15 months was assessed at 4.9 per cent., which compared with 11 per cent. in patients given a single injection of 2.4 mega units of procaine penicillin with aluminium monostearate. The method was shown to be successful in preventing infection of the infant in the treatment of eight pregnant syphilitic women.

In a series of 700 patients given a single injection of 2.4 mega units Bicillin the patient frequently complained of some slight pain and tenderness at the injection site appearing 8 to 12 hours after injection and continuing for 2 or 3 days, but no objective symptoms or local reactions were noted. Four of the patients developed dermatitis medicamentosa with severe pruritus, and two suffered marked anaphylactoid reactions. The incidence of significant reactions is assessed at about 1 per cent.

R. R. Willcox

Intravenous Terramycin in the Treatment of Early Syphilis and Granuloma Inguinale. DUNLOP, E. M. C., and ROBINSON, R. C. V. (1954). *Amer. J. Syph.*, **38**, 24. 14 refs.

In this paper from Johns Hopkins University and Hospital, Baltimore, the authors report their experience in the use of oxytetracycline given parenterally for the treatment of four confirmed cases of early syphilis and four of granuloma inguinale. Each patient was given 0.5 g. oxytetracycline dissolved in 250 ml. sterile water by intravenous drip over 10 to 15 minutes each day for 10 days. One patient complained of nausea during each

treatment and had a nitritoid reaction during the first treatment, while four others complained of diarrhoea, one of whom also had nausea after the first injection.

The results of treatment in the four cases of syphilis, which were followed up for 90 to 220 days, are given. In three of the four patients the result of dark-field examination for treponemes was still positive after 24 hrs, and in one patient it was positive after 48 hrs; this patient subsequently relapsed, returning with a lesion from which treponemata were recovered after 90 days. Healing was slow, and generalized lymph-node enlargement persisted for 3 months in one patient. In three of the patients there was a tendency to reversal of serological findings, and one sero-negative primary case, which became positive 13 days after treatment began, was again sero-negative after 220 days. Of the four cases of granuloma inguinale, which were followed up for periods of 56 to 122 days, two were healed, and two relapsed in 72 and 122 days respectively.

The authors conclude that the further use of oxytetracycline by intravenous infusion in the treatment of syphilis does not appear to be justified in view of the difficulty of administration and the proved efficacy of other modes of treatment, and that for the treatment of granuloma inguinale the intravenous administration of oxytetracycline in the dosage used does not seem to be so effective as other proved modes, including the oral administration of this drug.

Benjamin Schwartz

Corticotropin, Cortisone, Thyroid, Testosterone in Syphilitic Interstitial Keratitis. KLAUDER, J. V., and MEYER, G. P. (1954). *Arch. Ophthal. (Chicago)*, **51**, 432. 1 fig., 23 refs.

Holding the view that methods hitherto used in the treatment of syphilitic interstitial keratitis have not been successful in preventing industrial blindness in severe cases, the authors have tried corticotrophin, cortisone, thyroid extract, and testosterone, alone or in combination, in the treatment of this condition at the Wills Eye Hospital, Philadelphia. The total number of patients treated was 36, and of affected eyes 56, the disease being mild in eleven, moderate in seventeen, and severe in 28. In some cases all other treatment except myriatics was withheld during the administration of the above agents for the purposes of evaluation, but fever therapy and anti-syphilitic drugs were given sooner or later in all cases in the series.

Corticotrophin to a total dose of 450 to 670 mg. over a period of 9 to 15 days was given to three patients with the severe form of the disease; there was little, if any, improvement at the end of this period. Subconjunctival injections of 0.05 ml. of an aqueous suspension of cortisone containing 25 mg. per ml. were then given daily for 3 days to two of these three patients and to four others, a further course of three injections being given after several days' rest. There was no noticeable improvement, although only one of the six patients receiving cortisone in this way had a recurrence after subsequent treatment by other means. In thirteen cases cortisone acetate in a concentration of 25 mg. per ml. in a buffered phosphate

solution, with 1 in 5,000 benzalkonium chloride as a preservative and spreading agent, was used for local instillation, one drop being instilled into the conjunctival sac hourly during the day and 2-hourly during the night. In mild and moderate cases there was a dramatic clearing of the cornea and subsidence of the inflammation within 7 to 12 days, but in nine of the thirteen cases there was a recurrence on cessation of this treatment which was not prevented by the antisyphilitic therapy then being given. Since the basal metabolic rate was found to be uniformly low, desiccated thyroid, in a dosage of 2 to 3 gr. (0.13 to 0.2 g.) daily, was given in the remaining seventeen cases and also in twelve of the cases previously treated with cortisone. Administration was continued until improvement was noted, which was generally a few weeks to 2 months, and it is suggested that this treatment enhances the effect of fever and chemotherapy. Three patients received an intramuscular injection of 25 mg. testosterone *cyclo-pentylpropionate* each week for 6 weeks (in addition to other treatment) with little benefit.

The authors believe that some mechanism in the cornea, in all probability an immunological process in which vascularization is concerned, is responsible for regression of the disease, and that until the whole cornea has become vascular and the vessels meet in the centre (crisis), recovery will not take place. Cortisone does not assist this process, but retards it, and the authors have therefore discontinued its use.

Douglas J. Campbell

Comparative Effect of Various Antibiotics in Experimental Syphilis. TURNER, T. B., and SCHAEFFER, K. (1954). *Amer. J. Syph.*, **38**, 81. 49 refs.

At the International Treponematoses Laboratory Center, Baltimore, the antitreponemal effects of aureomycin, "terramycin" (oxytetracycline), chloramphenicol, streptomycin, erythromycin, and "magnamycin" (carbomycin) were compared in rabbits infected with the Nichols strain of *Treponema pallidum*. Penicillin was used as a standard of reference. All drugs were given by the intramuscular or intravenous route. All the antibiotics exhibited antitreponemal activity, but of a considerably lower order than that of penicillin. Although 103 animals were used, the number of experiments with any one antibiotic was too small to allow anything more than a rough comparison of treponemidal properties to be made. Within these limitations the order of effectiveness was found to be as follows:

- (1) penicillin;
- (2) carbomycin and erythromycin;
- (3) oxytetracycline and aureomycin;
- (4) chloramphenicol and streptomycin.

It is suggested that as carbomycin and possibly erythromycin appear to be the most likely substitutes for penicillin against syphilis, they should receive clinical trial. But it is clear that no other antibiotic at present available is in the same class as penicillin.

[This study also shows that the widespread use of these antibiotics for other conditions may, by their effect on *T. pallidum*, increase the difficulties of diagnosis and management in originally missed cases of syphilis.]

G. W. Csonka

Treatment of Neurosyphilis with Penicillin. GOTT, M. W. (1954). *Univ. Leeds med. J.*, **3**, 89. 2 refs.

Erb's Syphilitic Spinal Paralysis treated with Penicillin and Piromen. RAYPORT, M. (1954). *Neurology*, **4**, 517. 1 fig., 16 refs.

Treatment of Syphilis with Penicillin Alone. (Alleinige Penicillinbehandlung der Lues.) DÖLLKEN, H. (1954). *Z. Haut- u. GeschlKr.*, **17**, 46. 10 figs, 28 refs.

Penicillin by Oral Administration in the Prophylaxis and Abortive Treatment of Experimental Syphilis of Rabbits. KOLMER, J. A. (1954). *Amer. J. Syph.*, **38**, 176. 37 refs.

SYPHILIS (Serology)

Studies with the Treponemal Immobilizing Test. MILLER, J. L., SLATKIN, M. H., BRODEY, M., WECHSLER, H. L., and HILL, J. H. (1954). *J. Amer. med. Ass.*, **154**, 1241. 1 fig., 15 refs.

In this paper from Columbia University and the Presbyterian Hospital, New York, the results are given of a comparative investigation of the treponemal immobilization (T.P.I.) test and three standard serum tests for syphilis—the Mazzini, the V.D.R.L., and the Kolmer tests. In the first investigation sera from seventeen patients with early syphilis, thirty with early latent syphilis, 139 with late latent syphilis, 38 with neurosyphilis, and seven with cardiovascular syphilis were examined. With the exception of nine cases of early syphilis which had been treated 9 to 40 years previously, the T.P.I. test gave a positive reaction in all cases. It also gave a positive result with the cerebrospinal fluid of all of the 38 patients with neurosyphilis, whereas the standard tests were positive in only 26 of these cases.

Sera were also examined from a group of 162 patients who presented diagnostic problems. The diagnosis of syphilis was based on evidence other than the serological findings in only fourteen of these cases; the T.P.I. reaction was positive in all these fourteen, and in the whole group it was positive in 72 and negative in ninety. Of these ninety patients in whom the result was negative, 59 had received treatment for syphilis.

Parallel tests were carried out on selected patients admitted to hospital for a wide range of conditions other than syphilis, in many of whom the standard tests had given positive results. Among these, of fourteen patients with acute disseminated lupus erythematosus, eleven had positive or weakly positive reactions to the standard tests, whereas that to the T.P.I. test was negative in twelve, and in two cases the serum was too anticomplementary for a satisfactory test to be carried out. Of four patients with subacute disseminated lupus erythematosus, the standard tests gave positive or weakly positive reactions in three and the T.P.I. test in only one. Again, the standard tests gave positive results in four cases of discoid lupus erythematosus, and the T.P.I. test in only two of these. On the other hand, of twelve patients with

sarcoidosis, eleven gave positive or weakly positive response to the standard tests and ten to the T.P.I. test.

Evidence of the passive transfer of immobilizing antibody through the placenta was obtained on examination of 93 babies born of 74 mothers who had received varying types of treatment before or during pregnancy, of whom 55 had latent syphilis, eleven congenital syphilis, and four early syphilis; of the remainder, one had had yaws and three had given non-specific reactions. Only one baby showed signs of active syphilis, and its mother developed secondary syphilis post partum. Serial T.P.I. tests on seventy babies showed that while the passively transferred reagin disappeared from the child's blood by the 3rd month in 91 per cent. of cases, the immobilizing antibody persisted until the 4th or 5th month, usually disappearing by the 6th month.

The authors conclude that despite the diagnostic value of the T.P.I. test, it cannot be used as a guide to treatment, since no amount of treatment seems to alter it in patients who have not been adequately treated early in the infection. The test remains, however, the only practical procedure available for separating the group of false positive reactors from patients with latent syphilis. It is the authors' opinion that no one of the standard tests used is more valuable than any other in the diagnosis of syphilis, and that a high-titre reaction to the standard tests is not necessarily an indication of its specificity, since such reactions may be given by patients known to be false positive reactors. The T.P.I. test is especially helpful in the diagnosis of neurosyphilis, since the cerebrospinal fluid gives positive reactions in both the symptomatic and asymptomatic forms unless treatment has been given very early in the disease.

[This paper does not lend itself readily to abstracting because of the wide diversity of the clinical material studied, and should be read in the original by all those interested.]

A. E. Wilkinson

New Procedure for Evaluating Lecithin Preparations in Sero-Diagnostic Tests for Syphilis. SHARLIT, H., and REIN, C. R. (1954). *Amer. J. Syph.*, 38, 313.

Treponemal Antigen in the Sero-Diagnosis of Syphilis. (L'antigeno treponemico nella sierodiagnosi della lue.) GALLASSO, A. (1954). *G. Batt. Immun.*, 46, 470. 10 refs.

Treponemal Antigens in the Sero-Diagnosis of Syphilis. (Spirochäten-Antigene in der Serodiagnostik der Syphilis.) FROMM, G. (1954). *Arztl. Wschr.*, 9, 639. 11 refs.

Cardiolipin Complement-Fixation Test and the Pallida Reaction in the Clinical Problem of the Non-Specific Syphilitic Reaction. (Die Cardiolipin-Komplement-bindungsreaktion und die Pallida-Reaktion bei der Frage unspezifischer Luesreaktionen in der Klinik.) HENZE, S. (1954). *Medizinische*, 27-28, 949. 41 refs.

Studies of the *Treponema Pallidum* Immobilization (TPI) Test. IV. A Simplified Method of Preparing the Modified Basal Medium. AJELLO, G., PORTNOY, J., LOGAN, L., and OLANSKY, S. (1954). *Amer. J. Syph.*, 38, 288. 9 refs.

Syphilis Reservoir reduced by Serologic Surveys. LEE, S. S. (1954). *Publ. Hlth Rep. (Wash.)*, 69, 319.

SYPHILIS (Pathology)

Morphological and Histochemical Sequences in Syphilitic and in Tuberculous Orchitis in the Rabbit. SCOTT, V., and DAMMIN, G. J. (1954). *Amer. J. Syph.*, 38, 189. 10 figs, 10 refs.

***Treponema Pallidum* in Unstained Tissue Sections as seen under Dark-Ground Illumination.** COUTTS, W. E. (1954). *Indian J. vener. Dis.*, 20, 43. 1 ref.

SYPHILIS (Experimental)

Treponemal Immobilization Test during the Treatment of Experimental Syphilis with Penicillin and Bismuth. (Le test d'immobilisation des tréponèmes au cours du traitement de la syphilis expérimentale par l'association pénicilline-bismuth.) VAISMAN, A., HAMELIN, A., and DUNOYER, F. (1954). *Presse méd.*, 62, 829. 3 figs, 5 refs.

GONORRHOEA

Treatment of Gonorrhoea with Streptomycin. (Zur Behandlung der Gonorrhoe mit Streptomycin.) ZIERZ, P., and JACOB, R. (1954). *Hautarzt*, 5, 223. 1 fig, 35 refs.

The authors discuss the reasons which have prompted some workers to replace penicillin by streptomycin and other antibiotics in the treatment of gonorrhoea. These reasons have included the alleged frequent development of resistance to penicillin, the relative frequency of post-gonorrhoeal urethritis after treatment with the drug, and also the danger of masking the presence of associated syphilis, and it has been claimed that streptomycin is as efficacious as penicillin but without its disadvantages.

In a study undertaken by the authors at the University Dermatological Clinic, Heidelberg, to test this claim, 23 proved cases of gonorrhoea were treated with dihydrostreptomycin in doses of 0.5 g. once or twice daily or 1 g. once daily. The treatment failed completely in four cases owing to rapid development of resistance, but in the others serological reactions remained negative for 3 to 5 months after treatment.

The authors consider that the development of resistance to streptomycin is probably due to mutant strains, and is a serious disadvantage of this form of treatment. One strain in the series treated which became resistant to

streptomycin was also sensitive to penicillin, aureomycin, and sulphadiazine, and its resistance could not be diminished by the addition of a sub-optimal concentration of penicillin. They conclude that although streptomycin is no doubt extremely effective against the gonococcus, its use in the treatment of gonorrhoea cannot be recommended because of the rapid development of resistance.

Ferdinand Hillman

Complications of Gonorrhoea in the Antibiotic Era. (Über gonorrhoeische Komplikationen beim Manne in der antibiotischen Ära.) HÖFER, W. (1954). *Derm. Wschr.*, 129, 297. 13 refs.

The author reviews the incidence of complications in 2,000 cases of gonorrhoea in men treated with penicillin at the Municipal Clinic, Zwickau, Germany, during the years 1948-52. The results are compared with 500 cases treated with sulphonamides at the same clinic during the period 1946-48 and with results quoted in standard textbooks in the 1930s.

Clinically, of those treated with penicillin, 38 per cent. were cases of anterior urethritis and 62 per cent. of both anterior and posterior urethritis, compared with 24 and 72 per cent. respectively in the sulphonamide era. Among the complications of anterior urethritis, para-urethral infiltration occurred in 0.41 per cent. of penicillin-treated cases as against 1.13 per cent. in the earlier series; the para-urethral glands were found infected in 0.56 per cent. and there were four cases of acute inflammation of Cowper's glands. Chronic prostatitis occurred in up to 96 per cent. of topically treated cases in earlier days, but this figure fell to 50 per cent. in the author's sulphonamide-treated cases and to 30 per cent. in the penicillin era. Epididymitis was seen in 5.8 per cent. of the penicillin- and 6.6 per cent. of the sulphonamide-treated cases, these figures being compared with an incidence of between 6 and 58 per cent. in earlier reports. Vaginitis occurred in 33 per cent. and vesiculitis in 20 per cent. of the cases of epididymitis treated with penicillin. No cases of stricture were encountered.

The author concludes that certain complications of gonorrhoea, even when treated with penicillin, are still of importance. That they are less frequent than previously is due mainly to the shortening of the course of the disease which can be achieved by administration of penicillin and which results in most cases being cured before the complications can manifest themselves. Complications, when they do occur, usually respond to higher doses of penicillin.

Benjamin Schwartz

Relapses after Penicillin Treatment of Gonorrhoea in Practice. (Rückfälle nach Penicillinbehandlung der Gonorrhoe in der Praxis.) MARK, M. (1954). *Derm. Wschr.*, 129, 644. 5 refs.

NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS

Non-Gonococcal Urethritis treated with Aureomycin. JENSEN, T. (1954). *Amer. J. Syph.*, 38, 125. 3 figs, 22 refs.

At the Municipal Venereal Diseases Clinic, Copenhagen, 68 untreated cases of non-specific urethritis were given weekly injections of 1 ml. physiological saline (these acting as a control group), while 62 others were treated with aureomycin in the usual dosage of 1 to 2 g. daily for 3 or 4 days. Spontaneous recovery was noted in only 22 per cent. of the control group, whereas 66 per cent. of those receiving aureomycin were cured. An asymptomatic prostatitis was noted in 63 per cent. of cases.

An examination for pleuropneumonia-like organisms, made in 84 cases, showed these to be present in eighteen (21.7 per cent.). The presence of these organisms did not seem to be associated with a particular clinical course. These organisms were recovered from twelve (21.8 per cent.) of 55 aureomycin-treated patients and the condition in eleven of these twelve cases responded to treatment. Of the 43 aureomycin-treated cases in which such organisms were not found, a cure was obtained in only 28. The necessity for treating the consorts of patients with non-specific urethritis is emphasized.

R. R. Willcox

Non-Gonococcal Urethritis, with particular reference to the "Viral" Form. (Contributo allo studio delle uretriti non gonococciche con particolare riguardo alle cosiddette forme da virus Chlamydozoon oculogenitale e organismo "L".) TRIMIGLIOZZI, G. (1954). *Ann. ital. Derm. Sif.*, 9, 115. 32 refs.

Recovery of Pleuropneumonia-like Organisms from Negro Men with and without Non-Gonococcal Urethritis. SHEPARD, M. C. (1954). *Amer. J. Syph.*, 38, 113. 8 figs, 21 refs.

This investigation was carried out under the auspices of the U.S. Public Health Service at Duke University, Durham, North Carolina. By means of culture of urethral smears on Dienes's modification of Klieneberger's medium, pleuropneumonia-like organisms were recovered from twenty (53 per cent.) of 38 negro patients with non-specific urethritis, and in a larger group of 215 negro men attending venereal diseases clinics such organisms were found in 121 (56 per cent.). There was no relationship between the type of venereal disease and the incidence of the organisms. It is considered that men with venereal disease may be expected to harbour these organisms in the genito-urinary tract—not because they have venereal disease, but as a result of their sex-behaviour pattern.

In a group of 55 white medical students pleuropneumonia-like organisms were found in only one case (2 per cent.), while they were recovered from 19 (33 per cent.) of 57 apparently normal negro college students. No fundamental morphological differences could be detected between the organisms recovered from patients with non-specific urethritis and those from urethritis-free individuals such as would allow the recognition of possible pathogenic strains of these organisms.

[The results of this study support the modern view that although pleuropneumonia-like organisms may be genitally transmitted, they are not the usual cause of non-specific urethritis.]

R. R. Willcox

Significance of Bodies seen in Giemsa-Stained Urethral Scrapings in Non-Specific Urethritis. WILLCOX, R. R., HOWARD, E. M., and FINDLAY, G. M. (1954). *Amer. J. Syph.*, **38**, 216. 1 fig., 18 refs.

This report from the School of Pharmacy, London, describes the microscopical findings in the urethral scrapings taken from 250 men with non-specific urethritis, both before and after treatment with antibiotics, and compares them with those in scrapings from the urethral and cervical mucous membrane of 45 female consorts of the patients and in similar scrapings from control groups of subjects not suffering from urethritis but including 108 men recently successfully treated for gonorrhoea. All smears were stained with Giemsa's stain.

In the cases of non-specific urethritis, intra-epithelial granules and intra- and extra-epithelial granular bodies like minute clumps of frog spawn [which the authors term "colonies"] were seen in varying proportions of the specimens. Both granules and colonies might stain either red or blue with Giemsa's stain. It was found that the red-staining granules and colonies remained constant irrespective of treatment or of clinical improvement, but the blue-staining granules and colonies greatly decreased in number following successful treatment, increasing again if relapse occurred. Examination of scrapings from the female consorts showed similar colonies and granules in a proportion of the cases. In these cases, however, the structures stained blue did not disappear from the scrapings after treatment as they did in the male patients. Among eighty healthy men in the control groups blue granules or colonies were seen in very few cases. They were seen in about half the cases of recent gonococcal urethral infection, but the incidence declined as the urethra became drier. From this evidence the authors regretfully [but very reasonably] conclude that none of the bodies studied in this investigation are concerned with the causation of non-specific urethritis, but are most probably merely products of inflammation.

A. J. King

Researches in the Aetiology of Non-Specific Urethritis. WILLCOX, R. R. (1954). *Brit. med. J.*, **1**, 13.

The author reports the results of a search for a possible bacterial or viral cause of non-specific urethritis. First, a comparison was made between the bacterial flora found in urethral cultures from 105 controls [nature not stated] and that in 81 urethral cultures taken from patients with urethritis before treatment and 69 taken after treatment with orally administered antibiotics. As little difference was found between the flora in the three groups, it was concluded that "bacterial urethritis" was not a common entity.

In skin tests carried out with antigens of members of the psittacosis-lymphogranuloma venereum group of viruses seventeen urethritic patients and eleven controls gave negative results with psittacosis antigen; but eleven positive reactions were obtained with the antigen of lymphogranuloma venereum in 84 patients, compared with three in 62 control subjects. With the antigen of

cat-scratch fever two positive reactions in sixteen urethritic patients were observed, while twelve control patients all gave negative reactions. Complement-fixation tests with the antigen of lymphogranuloma venereum gave six positive results out of 141 samples of serum from patients, against three out of 132 control sera. Complement-fixation tests with the virus of enzootic abortion in ewes (thought to belong to the same group of viruses) gave four positive results in sera from 123 patients and five in sera from 127 controls.

Giemsa-stained smears of urethral scrapings from male patients were examined for inclusion bodies. Red- and blue-staining granules and granular "colonies" 1 to 6 μ in diameter were seen. An attempt was made to evaluate their significance by comparing their incidence in patients before treatment and after successful or unsuccessful treatment. The incidence of red granules and colonies was unaffected by treatment, suggesting that they were of no significance. Blue-staining granules and colonies, however, became fewer after successful treatment. Since they were also found in a proportion of urethral scrapings from patients with recently treated gonorrhoea, it was concluded that these bodies were merely products of inflammation. Attempts were also made to isolate a virus by inoculation of material into the lungs and brain of mice, into the conjunctiva, urethra, and knee-joint of baboons, subcutaneously into guinea-pigs, and into eggs by the chorio-allantoic route, but all failed to give any clear-cut evidence of an infective agent.

A. E. Wilkinson

Action of a New Antibiotic, Trichomycin, upon *Trichomonas vaginalis*, *Candida albicans*, and Anaerobic Bacteria. MAGARA, M., YOKOUTI, E., SENDA, T., and AMINO, E. (1954). *Antibiot. and Chemother.*, **4**, 433. 1 fig., 7 refs.

In this report from Nippon Medical College, Tokyo, the authors describe the results of a laboratory and clinical study of the new antibiotic, trichomycin, produced by *Streptomyces hachijoensis* and previously described by Hosoya and others (*Jap. J. exp. Med.*, 1952, **22**, 505). It was effective in concentrations of 0.01 mg. per ml. against *Trichomonas vaginalis*, and 0.0005 mg. of the antibiotic inhibited the growth of three strains of *Candida albicans* in 48 hours. It was also effective in inhibiting the growth of a small group of anaerobic bacteria, including a strain of *Clostridium perfringens*.

In the clinical tests the insertion of vaginal tablets containing 50 mg. trichomycin daily for 2 weeks in the treatment of patients with *Trichomonas* infection resulted in negative smears being obtained for 2 to 4 months, no toxic effects being observed. Similar treatment for seven doses caused amelioration of symptoms and negative smears in patients with vaginal moniliasis. Trichomycin had effect on aerobic bacteria such as *Staphylococcus* and *Streptococcus haemolyticus*.

D. Geraint James

Non-Gonococcal Urethritis treated with Aureomycin. JENSEN, T. (1954). *Acta derm.-venereol. (Stockh.)*, **34**, 82. 3 figs.

Orally-Administered Antibiotics in the Treatment of Non-Specific Urethritis. III. Oxytetracycline. WILLCOX, R. R. (1954). *Antibiot. and Chemother.*, 4, 173. 2 refs.

Incidence of Antibiotic-Resistant Staphylococci in Non-Gonococcal Urethritis. GROTON, W. M. (1954). *U.S. Armed Forces med. J.*, 5, 243. 12 refs.

Spirochaetal Prostatitis. (Beitrag zur Prostatitis spirochaetosa.) MÜLLER, L. (1954). *Derm. Wschr.*, 129, 620. 3 refs.

CHEMOTHERAPY

Oral Penicillin. FAIRBROTHER, R. W., and DABER, K. S. (1954). *Lancet*, 1, 858. 9 refs.

The authors review the results of previously published clinical trials of penicillin preparations administered orally. In view of the wide differences reported they have carried out a further study at the United Manchester Hospitals to determine the degree of absorption of penicillin after a single dose of various preparations administered by mouth.

In adults, 300,000 units of benzathine penicillin by mouth gave disappointing results. When the dose was increased to 600,000 units, however, a serum penicillin level of at least 0.03 unit per ml. was found in 67 of 68 tests within 3 hours, and at 5 or 6 hours 37 of 59 patients had levels of 0.06 unit per ml. or more, while in another eleven the level was 0.03 unit per ml. There was considerable individual variation, irrespective of the dosage. More uniform results were found in 31 children [no details are given of their ages or weights] with a dose of 300,000 units. After 2 or 3 hours the serum level was at least 0.25 unit per ml. in ten out of ten children; after 4 to 6 hours levels of 1 to 2 units per ml. were found in two infants, while in all of ten children the serum penicillin level exceeded 0.3 unit per ml. at this time. The levels were no higher after a dose of 600,000 units. In adults there was evidence of some cumulative effect of repeated doses of 600,000 units.

In a further test one of two preparations of soluble potassium benzylpenicillin was given to a group of 142 adults. Again results with a dose of 300,000 units were irregular, but after 600,000 units serum levels of from 0.03 to 1 unit per ml. were obtained in all of 58 patients at 1 to 3 hours, and similar levels were still present in thirty cases at 4 to 6 hours.

These results in general support the view that after the oral administration of penicillin absorption of the antibiotic is irregular and sometimes small. After a dose of 600,000 units there was, however, a peak serum penicillin level of at least 0.03 unit per ml. in most persons tested. The authors consider that in the treatment of acute infections the initial doses of penicillin should be given parenterally to ensure rapid bactericidal activity. It is emphasized that the blood penicillin level is not a direct index of therapeutic activity, others factors such as the

sensitivity of the organism being involved. As a minimum effective serum level of penicillin the figure of 0.03 unit per ml. has little therapeutic significance.

In conclusion, the authors urge that the ease of administration of penicillin by mouth should not lead to indiscriminate use of the antibiotic, especially in treating mild infections. Apart from the irregularity of absorption, notably in adults, oral treatment with penicillin is more expensive than parenteral injection of procaine penicillin, and one daily dose of the latter gives similar but more uniform serum levels.

[This is a valuable reminder of the need for caution in relying on the convenient method of giving penicillin by mouth in treatment of acute infections. It is interesting that absorption of the insoluble benzathine penicillin was no better and possibly less regular than that of the soluble potassium salt.]

Derek R. Wood

Benzathine Penicillin by Mouth in Children. BEASLEY, D. M. G., and MACPHERSON, M. J. (1954). *Lancet*, 1, 861. 1 fig., 5 refs.

In this investigation, carried out at the Children's Hospital, Sheffield, a preparation of benzathine penicillin ("Penidural") of which each 5 ml. contains 300,000 units of penicillin was given orally to 131 children divided into groups according to their weight. A serum penicillin concentration of 0.03 unit per ml. was taken as the minimum satisfactory level, and this level at least was usually observed one hour after administration. With a dose of 300,000 units, a satisfactory serum penicillin level was found 4 hours later in all of nineteen children weighing up to 40 lb. (18 kg.), and up to 6 hours later in eight children who weighed less than 25 lb. (11.3 kg.). Levels in heavier children, however, were unsatisfactory after this dose, but a dose of 600,000 units gave satisfactory levels at 4 hours in sixteen of seventeen children weighing between 40 and 70 lb. (18 and 32 kg.) and at 6 hours in seven out of nine children weighing between 25 and 40 lb. In children weighing over 40 lb., doses of 900,000 or 1,200,000 units were required to maintain satisfactory serum penicillin levels for 6 hours. Results observed in six cases showed that there was no significant accumulation of penicillin after repeated doses of 600,000 units every 4 hours in children weighing 40 lb. or more.

A scheme of dosage based on body weight is suggested. This indicates that 6-hourly doses of benzathine penicillin given orally should be about 12,000 units, and 4-hourly doses about 8,000 units, per lb. body weight (26,000 and 17,600 units respectively per kg.). The preparation was generally well tolerated, but 26 of the 131 children had loose stools and three had some nausea and vomiting.

[It is clear from the authors' detailed results that there was wide variation in the absorption of this substance from the intestine. No comparison was made with the results of potassium penicillin by mouth. The suggested dose schedule is a useful guide to dosage, but a blood level of 0.03 unit per ml. may not always be clinically effective, and other factors must be considered before relying on orally administered penicillin, even in

children. In Table I of the paper the symbol < used throughout should presumably be replaced by >, as used in Table II.]

Derek R. Wood

Binding of Penicillin in Relation to its Cytotoxic Action.

I. Correlation between the Penicillin Sensitivity and Combining Activity of Intact Bacteria and Cell-free Extracts. EAGLE, H. (1954). *J. exp. Med.*, **99**, 207, 4 figs, 11 refs.

A study of the action of penicillin upon bacteria and cell-free bacterial extracts was undertaken at the U.S. National Microbiological Institute, Bethesda, Maryland, the results of which confirm and extend the findings of Rowley and others (*Biochem. J.*, 1950, **46**, 157), who reported that the penicillin-binding activity of bacteria was correlated with their sensitivity to the drug.

The penicillin content of sensitive bacteria after exposure to the antibiotic consists of three fractions:

(a) freely diffusible penicillin, related to the fluid content of the bacteria;

(b) non-specifically-bound penicillin, present only after exposure to high concentrations of the antibiotic and readily removed by washing; and

(c) firmly bound penicillin, present after exposure to low concentrations (0.001 to 0.01 µg. per ml.) and not removed by washing.

When bacteria and cell-free extracts of bacteria disrupted by means of a sonic oscillator were exposed to penicillin labelled with radioactive sulphur (³⁵S) or carbon (¹⁴C) and the amount of firmly bound antibiotic determined, the affinity of both bacteria and extracts for penicillin was shown to be proportional to the penicillin sensitivity of the strain tested. Highly sensitive organisms such as *Streptococcus pyogenes* concentrated the antibiotic as much as 200-fold, but this did not occur if the penicillin had been inactivated by penicillinase or strong acids. Resting and multiplying organisms and cell-free extracts all reacted similarly to penicillin, suggesting that sensitivity does not depend upon differences in cell permeability. *B. coli* inactivated diffusible penicillin within the cell to a sufficient extent to explain its low binding affinity and relative resistance. Other species also inactivated penicillin within the cell, but only to a minor degree which was insufficient to explain their differences in penicillin sensitivity which, the author suggests, are "determined by differences in the reactivity of vital cell components with the antibiotic".

D. Geraint James

Stool Concentrations and Absorption of Chloramphenicol and its Palmitate in Babies. SPIERS, A. L. (1954). *Brit. J. Pharmacol.*, **9**, 59. 8 refs.

At Stobhill General Hospital, Glasgow, infants under the age of 15 months were given crystalline chloramphenicol or chloramphenicol palmitate, and the concentrations of the antibiotic in venous blood, stools, and urine were determined. Chloramphenicol was assayed biologically against the *El Tor* vibrio by serial dilution of inactivated and filtered preparations of stool and urine.

It was found that crystalline chloramphenicol was effectively absorbed, the levels in the serum and urine being high; the concentration in the stool was always low. The palmitate was poorly absorbed, the concentration in the stool being high though variable. The palmitate is therefore recommended for conditions in which there are pathogens in the lumen of the bowel, but not for infections of the tissues or the urinary tract.

L. G. Goodwin

Experimental Study on the Absorption of Oxytetracycline by the Stomach and the Small Intestine and its Excretion in the Bile. DANOPOULOS, E., ANGELOPOULOS, B., ZIOUDROU, C., and AMIRA, P. (1954). *Antibiot. and Chemother.*, **4**, 451. 6 figs, 3 refs.

It is well known that oxytetracycline when given by mouth is well absorbed by the gastro-intestinal tract. Experiments were carried out at the University of Athens to determine the rates of absorption by the stomach and by the small intestine separately, and also the amount of oxytetracycline excreted in the bile. It was found that when dogs were given oxytetracycline by mouth the greater part of the amount administered was absorbed by the stomach, a small part being retained by the liver to be excreted in the bile. In dogs with a biliary fistula the antibiotic was excreted in the bile in a concentration which was two to three times higher than the concentration in the blood. The maximum level in the bile occurred 3 to 6 hours after the antibiotic had been given. Clinical observations in one patient with postoperative biliary fistula confirmed these findings. The authors state that the antibiotic is concentrated in the liver, not the gall-bladder.

A. W. H. Foxell

Chloramphenicol and Haematopoiesis. Experimental Research on Chloramphenicol Poisoning in Guinea-pigs and on the Possible Therapeutic Action of the Vitamin-B Complex. (Cloramfenicolo ed emopoiesi. Ricerche sperimentali sull'intossicazione da cloramfenicolo nella cavia e sulla possibile attività riparatrice delle vitamine del gruppo B.) BALLERINI, G., and CASPANI, R. (1953). *Haematologica*, **37**, 1429. 4 figs, bibl.

In this paper from the University of Pavia the authors describe the results of investigations into the nature and prevention of the depressive action of chloramphenicol on haematopoiesis.

When twenty guinea-pigs were given 100 mg. chloramphenicol per kg. body weight daily for 16 days, two animals died and all the rest showed toxic effects—namely, anorexia, stupor, ruffled fur, and loss of weight. A further fifteen guinea-pigs were then given a similar dose of chloramphenicol, but after 12 days five were given vitamin B₁₂ (10 µg. per kg. daily), five folic acid (10 mg. per kg. daily), and five a preparation of the vitamin-B complex (2 ml. per kg. daily, this dose containing 10 mg. aneurin, 3 mg. riboflavin, 3 mg. pyridoxin, 100 mg. nicotinamide, and 10 mg. calcium pantothenate). Blood counts were made every 4 days and the bone marrow examined at the end of the experiment (28 days).

The results are given in detail. It is reported that chloramphenicol caused hypoplasia of the marrow cells, especially those of the erythropoietic series, which showed a cessation of maturation. These effects tended to be diminished in the animals treated with the vitamin-B complex, whereas folic acid and vitamin B₁₂ either had no effect or at the most produced only a limited response.

R. F. Jennison

Erythromycin in Venereal Diseases. ALEXANDER, L. J., and SCHOCH, A. G. (1954). *Amer. J. Syph.*, **38**, 107.

Penicillin in the Treatment of Chancroidal Bubo. JACKSON, T. F. M. (1954). *J. roy. Army med. Cps*, **100**, 151. 4 refs.

PUBLIC HEALTH AND SOCIAL ASPECTS

Detection of Infection Sources in Venereal Diseases. (Smitteopsporing ved kønssygdomme.) SPENDSER, K. (1954). *Nord. Med.*, **52**, 1021. 4 refs.

Correlation between Fluctuation in the Population and Venereal Disease. (Über die Korrelation zwischen Fluktuation und Geschlechtskrankheiten.) HARTUNG, J., and JANSSON, H. (1954). *Z. Haut- u. GeschlKr.*, **16**, 343. 1 fig., 9 refs.

Role of Psychology in the Conquest of V.D. RAYCHAUDHURY, A. K. (1954). *Indian J. vener. Dis.*, **20**, 44. 10 refs.

MISCELLANEOUS

Magnamycin in the Treatment of Granuloma Inguinale. ROBINSON, H. M., and COHEN, M. M. (1954). *J. invest. Derm.*, **22**, 263. 3 refs.

Six patients with granuloma inguinale were treated with magnamycin using enteric coated tablets. No relapses were noted. All six patients obtained a satisfactory result with complete healing of the lesions and no relapses occurred in a follow-up period from 1 to 3 months. No adverse reactions were encountered.

Magnamycin is of value in the treatment of granuloma inguinale. The optimum dose has not as yet been established. [Authors' summary.]

Outbreak of Pyogenic Penile Ulcers associated with a Microaerophilic Streptococcus resembling *Haemophilus ducreyi*. LEIBOVITZ, A. (1954). *Amer. J. Syph.*, **38**, 203. 29 refs.

The author noted an unusually high incidence of penile lesions resembling chancroid among United States troops

in Kyushu, Japan, during 1951 and early 1952. No fewer than 2,084 smears from penile lesions were examined during 1951 and 1,219 during early 1952, and in 63 per cent. of the earlier specimens and 47 per cent. of the later smears pyogenic organisms, including a microaerophilic streptococcus which closely resembled *Haemophilus ducreyi*, were found. In 367 cases in which both smears and cultures were examined, smears were positive for this organism in 45.8 per cent. of 825 examinations. In none of the cultures was *H. ducreyi* itself isolated, although in 35.15 per cent. the microaerophilic streptococcus was grown. Other pyogenic organisms, including diphtheroid bacilli and staphylococci, were found in many cases. A detailed study of the microaerophilic streptococcus was undertaken and is fully described.

Clinically, the incubation period of the penile ulcers varied from 2 to 10 days but was usually 3 to 5 days. They were situated beneath the prepuce in the majority (65 per cent.) of cases. In three-quarters of the cases the ulcer was single, and in was most instances from 3 to 5 mm. in diameter. The lesions were circular, with little or no induration, and those which were larger in size showed soft grey necrotic tissue irregularly disposed on the floor. All the ulcers were moderately tender but did not bleed easily. Moderate adenitis was present in 12 per cent. of the cases and was bilateral in about one-quarter of these. The ulcers resembled chancroids, but were less tender, more shallow, and spread more slowly, and the edges were seldom undermined.

Intradermal tests with vaccine of *H. ducreyi* were carried out in 42 cases, with positive results in fourteen. Auto-inoculation tests were negative for this organism and in most instances also for the microaerophilic streptococcus. From the results of this investigation the author concludes that smears from lesions and intradermal tests are of doubtful value in the diagnosis of chancroid.

A. J. King

Bacteriologic and Serologic Aspects of Pinta. REIN, C. R. (1954). *Amer. J. Syph.*, **38**, 336. 19 refs.

Dyschromia in Treponematoses. (Sur les Dyschromies des Treponematoses.) SILVA, J. RAMOS E., and GONÇALVES, A. P. (1954). *Act. dermo-sifilogr. (Madr.)*, **45**, 287. 28 refs.

Studies on Granuloma Inguinale. III. The Antigenic Heterogeneity of *Donovania Granulomatosis*. GOLDBERG, J. (1954). *Amer. J. Syph.*, **38**, 330. 2 refs.